REMARKS

Status of the Claims

Claims 16, 18, 31, 34, 36, 38, 40-42 and 45-47 are currently pending in the application. Claims 16, 18, 31, 34, 36, 38, 40-42 and 45-47 stand rejected. Claims 36 and 38 have been amended without prejudice or disclaimer. No new matter has been added by way of the present amendments. Specifically, the amendments to claim 36 is to remove heparin sulfate from the claim. Claim 38 is amended to address minor grammatical issues. Reconsideration is respectfully requested.

Provisional Request for Interview

Applicants believe the present amendments and comments place the present claims in condition for allowance. Should the claims be deemed not in condition for allowance, Applicants hereby provisionally request to conduct an interview with the Examiner to discuss the remaining issues precluding allowance, before the issuance of a further Office Action.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 16, 18, 31, 34, 36, 38, 40-42 and 45-47 stand rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the enablement requirement. (*See*, Office Action of March 11, 2008, at pages 2-6, hereinafter, "Office Action"). Applicants traverse the rejection.

The Examiner states that the claims are enabled for a DNA synthesis reaction composition comprising sulfated-fucose-containing polysaccharides (SFCPs) F and U at concentrations in the range of 0.02 to 5 ng/μL for amplification of DNA fragments up to 15 kb in

length, or a reaction composition comprising sodium alginate in the concentration range of 5-100 ng/μL for amplification of DNA fragments up to 12 kb in length. The Examiner states that the claims lack enablement for DNA synthesis reaction compositions comprising: hyaluronic acid, polyglutamic acid, polyacrylic acid, polystyrene sulfate, dematan sulfate or polyvinyl sulfate.

The Examiner maintains that Applicants' data and arguments are contradicted by the prior art, i.e. the disclosure of Peters, U.S. Patent Application Publication No. 2003/0092135 (hereinafter, "Peters"), which the Examiner states discloses that the claimed acidic substances inhibit PCR. The Examiner also cites other references which allegedly disclose data which the Examiner believes contradict Applicants' claims and data. Thus, rather than find only certain acidic substances as lacking enablement, the Examiner now states that all acidic substances recited in Applicants' claims, except SFCPs and sodium alginate, lack enablement because they are not believed to enhance DNA synthesis.

However, the Examiner's assertion or interpretation of the disclosure of Peters and the other cited references is incorrect, as explained below.

Peters does not disclose that PCR reactions are inhibited by polyanionic substances in general; rather, Peters discloses, at paragraphs [0145] - [0147] and in the Abstract, that PCR reactions are *improved* by the addition of polyanionic substances. For example, at paragraph [0145], the addition of dextran sulfate, which is a type of polyanion, remarkably improved the specificity of the PCR reaction. Peters states at paragraph [0145], "the addition of dextran sulfate Mw 4,000 significantly enhanced the specificity of the PCR reaction." At paragraph [0147], Peters states, "This example again illustrates that dextran sulfate 4,000 can be used in a concentration dependent manner to optimize both yield and specificity within a PCR reaction."

These statements appear to directly contradict the Examiner's interpretation of the disclosure of Peters. That is, Peters does not teach that polyanions are inhibitory to PCR, but rather supports enablement of the presently claimed invention.

While Demeke et al., *Biotechniques*, 12:332 and 334, 1992 (hereinafter, "Demeke et al."), which is cited at paragraph [0012] of Peters, may disclose an example wherein the addition of a specific acidic polysaccharide inhibits PCR amplification; in fact, Demeke et al. do not disclose that all acidic polysaccharides generally inhibit PCR amplification under all conditions. For example, at Table 1 in Demeke, the results of experiments on various acidic polysaccharides show that dextran sulfate and gum ghatti inhibit PCR reactions under conditions wherein the ratio of dextran sulfate/gum ghatti to template DNA is 500:1 (weight ratio). In contrast, at page 334, left column, lines 14-27 of Demeke et al., it is disclosed that the inhibitory effect of gum ghatti was not shown at lower ratios to DNA, such as at a ratio of 100:1 or lower. Also, it is disclosed in Demeke et al. that dextran sulfate did not inhibit the PCR reaction.

Thus, it appears the Examiner is overly generalizing the disclosures of Peters and Demeke et al. such that the disclosures themselves do not support the Examiner's overly general conclusions concerning all acidic polysaccharide substances.

Further, it is described at page 332, right column, line 27 to page 333, left column, and line 1 of Demeke et al. that even acidic polysaccharides inhibiting *Hin*dIII do not appear to inhibit PCR amplification. According to this description, even if a substance inhibited specific enzymes involved in nucleic acid amplification, the substance does not always, under all conditions, inhibit DNA amplification. Thus, the Examiner's overly generalized conclusions are again not sufficiently supported by these disclosures concerning the effects of acidic

polysaccharides on DNA amplification as shown in Wu et al. concerning Polynucleotide Kinase, and Do et al. concerning restriction endonucleases and Moelling et al. concerning retroviral reverse transcriptases, all of which are cited in Peters at paragraph [0012].

Additionally, the Examiner asserts that undue experimentation is necessary to achieve the enhancement of PCR by using the claimed compounds at all possible concentrations. This assertion is also unsupportable. After the invention was recognized by the Inventors, it merely requires routine experimentation for a person of skill in the art to determine a suitable or optimal concentration of the compounds claimed in the present invention, for enhancing PCR. This is true especially in light of the present disclosure and the concentration of polyanions disclosed in Demeke et al. which are shown to inhibit PCR.

For instance, it is disclosed at Example 6 in Peters, that the PCR yield and specificity are enhanced by addition of dextran sulfate, a conclusion which is entirely consistent with Applicants' observations, as disclosed in the present specification. Thus, Peters do not disclose any difficulties in using polyanions to enhance PCR reactions. Further, Applicants rely on the publication to support the enablement of the present invention, contrary to the Examiner's position.

Furthermore, it is noted that those acidic substances believed by the Examiner to show inhibitory effects, specifically dextran sulfate, gum ghatti and heparin, have been deleted from the pending claims.

As described above, the claims of the present application are believed to fully satisfy the enablement requirement.

Therefore, reconsideration and withdrawal of the enablement rejection of claims 16, 18, 31, 34, 36, 38, 40-42 and 45-47 are respectfully requested.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claim 38 stands rejected under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. (*See*, Office Action, at pages 6-7). Applicants traverse the rejection as set forth herein.

The Examiner states that the phrase "said DNA polymerase is thermostable" is indefinite. The Examiner states that it is unclear which of the two DNA polymerases from claim 36 (from which claim 38 depends) this phrase is referring to.

Although Applicants do not agree that claim 38 is indefinite, to expedite prosecution, claim 38 has been amended to recite, "The kit according to claim 36, wherein at least one of said two or more kinds of DNA polymelases is thermostable." Applicants believe this amendment clarifies which of the two DNA polymerases from claim 36 to which claim 38 is referring.

Reconsideration and withdrawal of the indefiniteness rejection of claim 38 are respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Claims 36 and 38 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Al-Soud et al., *Applied Env. Microbiol.*, 64:3748-3753, 1998 (hereinafter, "Al-Soud et al.") as evidenced by Wikipedia entry for Heparin Sulfate dated April 21, 2007 and Stratagene Catalog,

page 39, 1988. (*See*, Office Action, at pages 7-8). Applicants traverse the rejection as hereinafter set forth.

The Examiner states that Al-Soud et al. disclose a composition comprising two thermostable DNA polymerases, having the activities recited in the present claims, and components necessary for DNA synthesis including animal tissue. The Examiner states that heparin sulfate is known to be found in animal tissue (as evidenced by the entry for heparin sulfate on the Wikipedia website). The Examiner admits that Al-Soud et al. do not disclose kits comprising these components. However, the Examiner cites to Strategene catalog of 1988 which discloses that combining reagents into kit form is useful.

Although Applicants do not agree that claims 36 and 38 are obvious in light of the cited references, to expedite prosecution, claim 36 has been amended herein to delete the term "heparin sulfate" from the claim. Thus, it is believed that Al-Soud et al. no longer discloses all of the limitations which are encompassed by at least amended claim 36.

Since no specific reasoning is provided by the Examiner for the rejection of dependent claim 38, dependent claim 38 is also believed to not be obvious in light of the cited references for, *inter alia*, depending from a non-obvious base claim, amended independent claim 36.

Reconsideration and withdrawal of the obviousness rejection of claims 36 and 38 are respectfully requested.

CONCLUSION

If the Examiner has any questions or comments, please contact Thomas J. Siepmann, Ph.D., Registration No 57,374, at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

Dated: July 11, 2008

Respectfully submitted,

By _____

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